Claims

1. A method of diagnosing a cancer, comprising:

contacting a non-testis biological sample isolated from a subject with an agent that specifically binds to a nucleic acid molecule, an expression product thereof, or a fragment of the expression product thereof complexed with an HLA molecule, wherein the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, and

determining the interaction between the agent and the nucleic acid molecule or the expression product to diagnose the cancer in the subject.

2. The method of claim 1, wherein the agent is selected from the group consisting of

(a) a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22 or a fragment thereof,

(b) an antibody that binds to an expression product of a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, and

(c) an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

3. The method of claim 1, wherein the cancer is characterized by expression of a plurality of human CT antigen precursors and wherein the agent is a plurality of agents, each of which is specific for a different human CT antigen precursor, and wherein said plurality of agents is at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8, at least 9 or at least 10 such agents.

4. A method of diagnosing a cancer, comprising:

contacting a non-testis, non-brain biological sample isolated from a subject with an agent that specifically binds to a nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an HLA molecule, wherein the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO:32, and

determining the interaction between the agent and the nucleic acid molecule or the expression product to diagnose the cancer in the subject.

5. A method of diagnosing a cancer, comprising:

contacting a non-testis, non-ovary, non-cervix, non-lung biological sample isolated from a subject with an agent that specifically binds to a nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an HLA molecule, wherein the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO:34, and

determining the interaction between the agent and the nucleic acid molecule or the expression product to diagnose the cancer in the subject.

6. A method of diagnosing a cancer, comprising:

contacting a non-testis, non-ovary, non-lung, non-breast, non-prostate, non-colon biological sample isolated from a subject with an agent that specifically binds to a nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an HLA molecule, wherein the nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO:36, and

determining the interaction between the agent and the nucleic acid molecule or the expression product to diagnose the cancer in the subject.

7. A method for determining regression, progression or onset of a cancer characterized by expression of abnormal levels of a protein encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, comprising

monitoring a plurality of non-testis samples obtained at different times from a subject who has or is suspected of having the cancer, for a parameter selected from the group consisting of

(i) the protein,

(ii) a peptide derived from the protein,

(iii) an antibody which selectively binds the protein or peptide,

(iv) cytolytic T cells specific for a complex of the peptide derived from the protein and an MHC molecule, and

(v) a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22; and

comparing the parameters from the plurality of samples to determine regression, progression or onset of the cancer.

8. The method of claim 7, wherein the sample is a body fluid, a body effusion, cell or a tissue.

9. The method of claim 7, wherein the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of

(a) an antibody which selectively binds the protein of (i), or the peptide of (ii),

(b) a protein or peptide which binds the antibody of (iii),

(c) a cell which presents the complex of the peptide and MHC molecule of (iv), and

(d) at least one nucleic acid probe or primer that hybridizes to the nucleic acid molecule of (v) or its complement.

10. The method of claim 9, wherein the antibody, the protein, the peptide, the cell or the nucleic acid probe or primer is labeled with a radioactive label or an enzyme.

11. The method of claim 7, wherein the protein is a plurality of proteins, the parameter is a plurality of parameters, each of the plurality of parameters being specific for a different of the plurality of proteins, at least one of which is a CT antigen protein encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

12. A pharmaceutical preparation for a human subject comprising

an agent which when administered to the subject enriches selectively the presence of complexes of an HLA molecule and a human CT antigen peptide, and

a pharmaceutically acceptable carrier, wherein the human CT antigen peptide is a fragment of a human CT antigen encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

13. The pharmaceutical preparation of claim 12, wherein the agent comprises a plurality of agents, each of which enriches selectively in the subject complexes of an HLA molecule and a different human CT antigen peptide, wherein at least one of the human CT antigens is encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

14. The pharmaceutical preparation of claim 12, wherein the agent is selected from the group consisting of

(1) an isolated polypeptide comprising the human CT antigen peptide,

(2) an isolated nucleic acid operably linked to a promoter for expressing the isolated polypeptide,

(3) a host cell expressing the isolated polypeptide, and

(4) isolated complexes of the polypeptide, and an HLA molecule.

15. The pharmaceutical preparation of claims 12-14, further comprising an adjuvant.

16. The pharmaceutical preparation of claim 12, wherein the agent is a cell expressing an isolated polypeptide comprising the human CT antigen peptide, and wherein the cell is nonproliferative.

17. The pharmaceutical preparation of claim 12, wherein the agent is a cell expressing an isolated polypeptide comprising the human CT antigen peptide, and wherein the cell expresses an HLA molecule that binds the polypeptide.

18. The pharmaceutical preparation of claim 17, wherein the cell expresses one or both of the polypeptide and HLA molecule recombinantly.

19. The pharmaceutical preparation of claim 17, wherein the cell is nonproliferative.

20. A composition comprising

an isolated agent that binds selectively a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:21, 23, 25, 27, 29, 31, 35 and 37.

21. The composition of matter of claim 20, wherein the agent is an antibody or an antigen-binding fragment thereof.

22. The composition of claim 21, wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

23. A composition of matter comprising a conjugate of the agent of claims 20 or 21 and a therapeutic or diagnostic agent.

24. The composition of matter of claim 23, wherein the conjugate is of the agent and a therapeutic or diagnostic that is a toxin.

25. A pharmaceutical composition comprising

an isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, and

a pharmaceutically acceptable carrier.

26. The pharmaceutical composition of claim 25, wherein the isolated nucleic acid molecule comprises at least two isolated nucleic acid molecules coding for two different polypeptides, each polypeptide comprising a different human CT antigen.

27. The pharmaceutical composition of claims 25 or 26 further comprising an expression vector with a promoter operably linked to the isolated nucleic acid molecule.

28. The pharmaceutical composition of claims 25 or 26 further comprising a host cell recombinantly expressing the isolated nucleic acid molecule.

29. A pharmaceutical composition comprising

an isolated polypeptide comprising a polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, and

a pharmaceutically acceptable carrier.

30. The pharmaceutical composition of claim 29, wherein the isolated polypeptide comprises at least two different polypeptides, each comprising a different human CT antigen.

31. The pharmaceutical composition of claims 29 or 30, further comprising an adjuvant.

32. A protein microarray comprising at least one polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, or an antigenic fragment of the polypeptide.

33. The microarray of claim 32, wherein the at least one polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:19, 21 and 23.

34. A protein microarray comprising at least one polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:24, 26, 28 and 30, or an antigenic fragment of the polypeptide.

35. The microarray of claim 34, wherein the at least one polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:25, 27, 29 and 31.

36. A protein microarray comprising at least one polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:32, 34 and 36, or an antigenic fragment of the polypeptide.

37. The microarray of claim 36, wherein the at least one polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:33, 35 and 37.

38. A protein microarray comprising a plurality of antibodies or antigen-binding fragments thereof that specifically bind at least one polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, or an antigenic fragment of the polypeptide.

39. The microarray of claim 38, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:19, 21 and 23.

40. A protein microarray comprising a plurality of antibodies or antigen-binding fragments thereof that specifically bind at least one polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:24, 26, 28 and 30, or an antigenic fragment of the polypeptide.

41. The microarray of claim 40, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:25, 27, 29 and 31.

42. A protein microarray comprising a plurality of antibodies or antigen-binding fragments thereof that specifically bind at least one polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:32, 34 and 36, or an antigenic fragment of the polypeptide.

43. The microarray of claim 42, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:33, 35 and 37.

44. A nucleic acid microarray comprising at least one nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, or a fragment thereof of at least 20 nucleotides that selectively hybridizes to its complement in a biological sample.

45. A nucleic acid microarray comprising at least one nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:24, 26, 28 and 30, or

a fragment thereof of at least 20 nucleotides that selectively hybridizes to its complement in a biological sample.

46. A nucleic acid microarray comprising at least one nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:32, 34 and 36, or a fragment thereof of at least 20 nucleotides that selectively hybridizes to its complement in a biological sample.

47. An isolated fragment of a human CT antigen which, or a portion of which, binds a HLA molecule or a human antibody, wherein the CT antigen is encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

48. The fragment of claim 47, wherein the fragment is part of a complex with the HLA molecule.

49. The fragment of claim 47, wherein the fragment is between 8 and 12 amino acids in length.

50. A kit for detecting the expression of two or more human CT antigens comprising two or more pairs of isolated nucleic acid molecules, each of which consists essentially of a nucleic acid molecule selected from the group consisting of (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence of any of SEQ ID NOs:18, 20 or 22, and (b) complements of (a), wherein the contiguous segments are nonoverlapping, and wherein the nucleic acid molecules in each of the pairs are specific for a human CT antigen.

51. The kit of claim 50, wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify at least a fragment of an isolated nucleic acid molecule selected from the group consisting of SEQ ID NOs:18, 20 and 22.

52. A method for treating a subject with a cancer characterized by expression of a human CT antigen, comprising

administering to the subject an amount of an agent, which enriches selectively in the subject the presence of complexes of a HLA molecule and a human CT antigen peptide, effective to ameliorate the disorder, wherein the human CT antigen peptide is a fragment of a human CT antigen encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

53. The method of claim 52, wherein the cancer is characterized by expression of a plurality of human CT antigens and wherein the agent is a plurality of agents, each of which enriches selectively in the subject the presence of complexes of an HLA molecule and a different human CT antigen peptide, wherein at least one of the human CT antigens is encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

54. The method of claim 52, wherein the agent is an isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

55. A method for treating a subject having a cancer characterized by expression of a human CT antigen in cells of the subject, comprising:

(i) removing an immunoreactive cell containing sample from the subject,

(ii) contacting the immunoreactive cell containing sample to the host cell under conditions favoring production of cytolytic T cells against a human CT antigen peptide that is a fragment of the human CT antigen,

(iii) introducing the cytolytic T cells to the subject in an amount effective to lyse cells which express the human CT antigen, wherein the host cell is transformed or transfected with an expression vector comprising an isolated nucleic acid molecule operably linked to a promoter, wherein the isolated nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

56. The method of claim 55, wherein the host cell recombinantly expresses an HLA molecule which binds the human CT antigen peptide.

57. The method of claim 55, wherein the host cell endogenously expresses an HLA molecule which binds the human CT antigen peptide.

58. A method for treating a subject having a cancer characterized by expression of a human CT antigen in cells of the subject, comprising:

(i) identifying a nucleic acid molecule expressed by the cells of the cancer, wherein the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, or a fragment thereof;

(ii) transfecting a host cell with a nucleic acid molecule selected from the group consisting of (a) the nucleic acid molecule identified, (b) a fragment of the nucleic acid identified which includes a segment coding for a human CT antigen, (c) degenerates of (a) or (b);

(iii) culturing said transfected host cells to express the transfected nucleic acid molecule, and;

(iv) introducing an amount of said host cells or an extract thereof to the subject effective to increase an immune response against the cells of the subject associated with the condition.

59. The method of claim 58, further comprising identifying an MHC molecule which presents a portion of an expression product of the nucleic acid molecule, wherein the host cell expresses the same MHC molecule as identified and wherein the host cell presents an MHC binding portion of the expression product of the nucleic acid molecule.

60. The method of claim 58, wherein the immune response comprises a B-cell response or a T cell response.

61. The method of claim 60, wherein the response is a T-cell response which comprises generation of cytolytic T-cells specific for the host cells presenting the portion of the expression product of the nucleic acid molecule or cells of the subject expressing the human CT antigen.

62. The method of claim 58, wherein the nucleic acid molecule is selected from the group consisting of SEQ ID NOs:18, 20 and 22.

63. The method of claims 58 or 59, further comprising treating the host cells to render them non-proliferative.

64. A method for treating or diagnosing or monitoring a subject having a cancer characterized by expression of a protein encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20, and 22, in cells or tissues other than testis, comprising

administering to the subject an antibody which specifically binds to the protein or a peptide derived therefrom, the antibody being coupled to a therapeutically or diagnostically useful agent, in an amount effective to treat, diagnose or monitor the condition.

65. The method of claim 64, wherein the antibody is a monoclonal antibody or an antigen-binding fragment thereof.

66. The method of claim 65, wherein the monoclonal antibody is a chimeric antibody or a humanized antibody.

67. A method for treating a cancer characterized by expression of a protein encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, in cells or tissues other than testis, comprising

administering to a subject a pharmaceutical composition of any one of claims 12-19 and 25-31 in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject.

68. The method of claim 67, further comprising first identifying that the subject expresses abnormal amounts of the protein in a non-testis tissue.

69. A method for treating a subject having a cancer characterized by expression of a protein encoded by a nucleic acid molecule comprising a nucleotide sequence selected from

the group consisting of SEQ ID NOs:18, 20 and 22, in cells or tissues other than testis, comprising

(i) identifying cells from the subject which express abnormal amounts of the protein;

(ii) isolating a sample of the cells;

(iii) cultivating the cells, and

(iv) introducing the cells to the subject in an amount effective to provoke an immune response against the cells.

70. The method of claim 69, further comprising rendering the cells non-proliferative, prior to introducing them to the subject.

71. A method for treating a pathological cell condition characterized by expression of a protein encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22, in cells or tissues other than testis, comprising

administering to a subject in need thereof an effective amount of an agent which inhibits the expression or activity of the protein.

72. The method of claim 71, wherein the agent is an inhibiting antibody which selectively binds to the protein and wherein the antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody or an antibody fragment.

73. The method of claim 71, wherein the agent is an antisense nucleic acid molecule which selectively binds to the nucleic acid molecule which encodes the protein.

74. A composition of matter useful in stimulating an immune response to a plurality of a proteins comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:19, 21 and 23 comprising

a plurality of peptides that are fragments of the proteins, wherein the peptides bind to one or more MHC molecules presented on the surface of non-testis cells.

75. The composition of matter of claim 74, wherein at least a portion of the plurality of peptides bind to MHC molecules and elicit a cytolytic response thereto.

76. The composition of matter of claim 74, wherein at least one of the proteins is encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20 and 22.

77. The composition of matter of claim 74, further comprising an adjuvant.

78. The composition of matter of claim 77, wherein said adjuvant is selected from the group consisting of saponins, GM-CSF, interleukins, and immunostimulatory oligonucleotides.

79. An isolated antibody which selectively binds to a complex of:

(i) a peptide that is a fragment of a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:19, 21 and 23, and

(ii) a MHC molecule to which binds the peptide to form the complex, wherein the isolated antibody does not bind to (i) or (ii) alone.

80. The antibody of claim 79, wherein the antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, or an antigen-binding fragment thereof.

81. A method for treating or diagnosing or monitoring a subject having a cancer characterized by expression of a protein encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20, and 22, in cells or tissues other than testis, comprising

administering to the subject the antibody of claim 79, the antibody being coupled to a therapeutically or diagnostically useful agent, in an amount effective to treat, diagnose or monitor the condition.

82. A method for treating or diagnosing or monitoring a subject having a cancer characterized by expression of a protein encoded by a nucleic acid molecule comprising a

nucleotide sequence selected from the group consisting of SEQ ID NOs:18, 20, and 22, in cells or tissues other than testis, comprising

administering to the subject the antibody of claim 80, the antibody being coupled to a therapeutically or diagnostically useful agent, in an amount effective to treat, diagnose or monitor the condition.